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The Association between Cholecystectomy and Gastroesophageal Reflux Symptoms: A Prospective Controlled Study

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Abstract

Objective—A large controlled prospective observational study to compare pre- and post-surgery changes in reflux symptoms between cholecystectomy and hernia repair surgery patients.

Summary Background Data—Six studies have suggested that gastroesophageal reflux worsens after cholecystectomy. However, these studies all had design limitations.

Methods—We recruited 302 patients scheduled to undergo elective cholecystectomy (study group) or hernia repair (controls) at two hospitals. Both groups filled out the validated Reflux Symptom Score (RSS) and Gastrointestinal Symptom Rating Scale (GSRS) questionnaires 1–15 days prior to and 4–12 weeks after the operation. Changes in symptom scores between the pre and post-surgery assessments were measured, and compared between the two groups.

Results—Baseline RSS and GSRS reflux subscores were higher in the study group than controls (1.44 vs. 1.02 and 1.91 vs. 1.43 respectively; $p < 0.05$). There were no significant differences in any of the symptom score changes between the two groups except for the GSRS pain subscore, which decreased more in the study group than the control group (-0.59 vs. -0.10 ; $p < 0.001$). With regard to reflux, the RSS decreased by -0.34 in the study group and -0.14 in controls ($p = 0.27$), while the GSRS reflux subscore decreased by -0.32 in the study group and -0.05 in controls ($p = 0.12$). GSRS diarrhea and constipation subscores decreased slightly after surgery, to the same extent in both groups.

Conclusions—This large prospective controlled study, the only one using validated reflux symptom questionnaires, shows that cholecystectomy does not lead to an increase in reflux symptoms. As expected, GSRS pain subscores were decreased in the cholecystectomy group but not the controls.

Keywords

Cholecystectomy; gastroesophageal reflux; hernia repair

Introduction

It has been anecdotally noted that gastroesophageal reflux symptoms can be worsened by cholecystectomy. The mechanism of this possible association is unclear, but may be related to a variety of processes involving impaired gastric motility, lower esophageal sphincter function or duodenogastric reflux following cholecystectomy. Six previous studies have suggested that gastroesophageal reflux worsens after cholecystectomy¹⁻⁶. However, these studies were either uncontrolled or retrospective, and many used unvalidated symptom questionnaires and had small sample sizes. The only prospective controlled study to date did not show that reflux worsened after cholecystectomy⁷, but its sample size was very small. We performed a large controlled prospective observational study on patients undergoing elective cholecystectomy or surgical hernia repair, using validated questionnaires to compare pre- and post-surgery changes in reflux and other gastrointestinal symptom scores between the two groups.

Methods

This was a prospective controlled study performed at Virginia Mason Medical Center (VMMC) and Stanford University Medical Center (SUMC). This study protocol was approved by the Institutional Review Boards of the two hospitals. All subjects signed informed consent.

Subject Selection

Eligible adult patients scheduled for elective laparoscopic cholecystectomy for cholelithiasis at VMMC and SUMC were prospectively recruited. Concurrent control patients scheduled for elective inguinal hernia repair at these two institutions were also enrolled.

Exclusion criteria included the following: serious complications from the surgery that resulted in extension of the hospitalization; any history of gastrectomy, vagotomy, esophageal surgery, pyloroplasty, biliary surgery, or liver surgery; serious concurrent gastrointestinal illnesses, such as gastrointestinal tract, biliary or hepatic tumors, active peptic ulcer disease, advanced liver failure, esophageal strictures, inflammatory bowel disease or ischemic bowel disease; other surgical resections, except for lymph node biopsies, done during the operation. Patients who underwent cholecystectomy for gallbladder or biliary cancer were excluded.

Data Collection

Reflux and other gastrointestinal symptoms were measured using the Reflux Symptom Score (RSS)⁸ and Gastrointestinal Symptom Rating Scale (GSRS)⁹. The RSS has been validated in large population studies⁸. It consists of three direct questions, asking about the symptoms (heartburn or regurgitation, with scores ranging from 0 to 1.5), the presence of nocturnal heartburn or regurgitation (score of 2 for an affirmative answer), and the frequency of heartburn or regurgitation occurrence (with scores ranging from 0 for less than once per week to 3 for >15 times per week). The RSS is simply the sum of the scores for the 3 questions, and can range from 0 to 6.5. Thus, a patient with both heartburn and regurgitation symptoms that occur >15 times per week, with a nocturnal component, would receive a maximum RSS of 6.5. The GSRS has also been extensively validated⁹, and consists of 15 items, the responses to which are combined to give five subscores, reflecting reflux, indigestion, pain, diarrhea and constipation symptoms. Two of the items are specific to reflux disease, referring to heartburn and regurgitation. Patients express their agreement with each statement using a score from 1–7, and the subscore for each category is derived by averaging the individual scores for all items in that symptom category. For example, the

reflux subscore would be derived by adding the scores for the two reflux items and then dividing by two. Thus, a patient who gave a score of 7 for both reflux items would receive a GSRS reflux subscore of 7.

Each subject filled out the RSS and GSRS questionnaires 1–15 days prior to surgery, then filled out the same questionnaires again 4–12 weeks after the surgery. Changes in symptom scores before and after the surgery in the cholecystectomy and hernia groups were measured, and these changes were compared between the two groups. Demographic and other background data collected by questionnaire at the time of the initial survey included smoking habits, alcohol ingestion, caffeine intake, medication profile, and comorbid illnesses (if any). If the patient had undergone upper endoscopy within two years prior to the surgery, the findings were also noted.

Statistical Analysis

Prior to commencement of our study, a power calculation showed that a total sample size of 300 would give an estimated detectable RSS difference of approximately 0.2 for a power of 80% at the 0.05 significance level (using the unpaired Student t-test). This compared favorably with the magnitude of pH changes seen in previous studies ².

Comparative testing between the study and control groups was done using the unpaired 2-tailed Student t test or chi-squared test. Comparative testing between the pre- and post-surgery scores was done using the paired 2-tailed Student t test or chi-squared test. For the five GSRS subscores, Bonferroni corrections for multiple comparisons were done by multiplying the raw p-values by 5. P-values <0.05 were considered significant. We also performed stratified analysis on patients with no baseline reflux (RSS of 0 or GSRS reflux subscore of 1) and those with baseline reflux symptoms (RSS>0 or GSRS reflux subscore >1).

Multivariate linear and logistic regression analyses were performed using many of the collected demographic and other background variables. Statistical analysis was done using SPSS 13.0 (SPSS Inc., Chicago, Illinois).

Results

We prospectively enrolled 321 subjects, including 125 cholecystectomy patients (98 from VMMC; 27 from SUMC) and 196 hernia surgery controls (145 from VMMC; 51 from SUMC). Of the cholecystectomy patients, 121 underwent laparoscopic cholecystectomy as planned, while 4 required conversion to open cholecystectomy.

Patient Characteristics

Compared with the cholecystectomy patients, the hernia control group was slightly older (mean age 59.0 vs. 54.6 years; $p=0.008$), and had a much higher proportion of males (81.6% vs. 36.8%; $p<0.001$). Smoking history and alcohol intake were not different between the two groups (Table 1). The hernia patients consumed larger quantities of caffeine, and the proportion of cholecystectomy patients regularly taking acid suppressive medications (proton pump inhibitors or histamine receptor blockers) was slightly higher (27% vs. 17%; $p=0.04$). There was no difference in the proportion of patients with various comorbid conditions (Table 1). The age and gender distributions between the VMMC and SUMC patients were similar (data not shown). Of the cholecystectomy patients, 34% had undergone upper endoscopy within two years of surgery, versus only 16% of the hernia patients ($p<0.001$); however, the prevalence of erosive esophagitis or Barrett's esophagus in those who had endoscopy was not significantly different between the cholecystectomy and hernia groups (10% vs. 15%; $p=0.21$).

RSS Scores

Table 2 shows RSS data. Baseline presurgical RSS values were slightly higher in the cholecystectomy group than the hernia group (1.44 vs. 1.02; $p=0.04$). Post-surgical RSS values were statistically similar in the two groups (1.10 vs. 0.88; $p=0.23$). On average, the RSS score decreased by -0.34 in the cholecystectomy group and -0.14 in the hernia group ($p=0.27$). About 35% of cholecystectomy patients exhibited a drop in RSS after the surgery; the remainder showed no change or a rise in RSS. Increases in RSS were generally smaller in magnitude than decreases in RSS, thus the mean change in RSS for the entire group was negative. For the controls, 39% had a drop in RSS after surgery, resulting in no significant differences in the proportion of patients with RSS decreases between the cholecystectomy and hernia groups ($p=0.52$).

Given the markedly different gender compositions in the two groups, we stratified the data by gender. At baseline, RSS values were generally higher in cholecystectomy patients than hernia patients for men but not women (for men, 1.59 vs. 0.89; $p=0.03$; for women, 1.35 vs. 1.62; $p=0.51$). For men, the RSS decreased by -0.23 in the cholecystectomy group and -0.06 in the hernia group ($p=0.45$). For women, the RSS score decreased by -0.41 in the cholecystectomy group and -0.52 in the hernia group ($p=0.79$). Thus, even when stratified by gender, there was still no difference in the change in RSS values between the cholecystectomy and hernia groups. We also found no significant difference in RSS changes if we stratified the results by hospital (data not shown).

When we stratified the data according to whether or not patients had baseline reflux, we found that a slightly higher proportion of control patients had no baseline reflux symptoms compared with cholecystectomy patients (62% vs. 50%; $p=0.04$). Patients with no baseline reflux symptoms, who started off with an RSS of 0, exhibited a slight rise in RSS after surgery ($+0.35$ for cholecystectomy and $+0.36$ for hernia surgery; $p<0.01$ for both). In contrast, patients with baseline reflux symptoms, who started off with an RSS >0 , showed a significant drop in RSS after surgery (-1.10 for cholecystectomy and -1.09 for hernia surgery; $p<0.001$ for both). However, there were no significant differences when we compared pre and post-surgery changes between the cholecystectomy and control groups ($p=0.95$ for patients without baseline reflux; $p=0.98$ for patients with baseline reflux).

GSRS Subscores

Table 3 shows data on GSRS subscores. Baseline GSRS reflux subscores were higher in the cholecystectomy group than the controls (1.91 vs. 1.43 respectively; $p<0.001$). Not surprisingly, GSRS pain subscores were also higher in the cholecystectomy group than the controls (2.34 vs. 1.59; $p<0.001$), as were GSRS indigestion subscores (2.32 vs. 1.89; $p=0.002$). After surgery, reflux and pain subscores decreased in both groups of patients, but the pain subscore remained higher in the cholecystectomy group (1.76 vs. 1.50; $p=0.004$). There were no statistically significant differences in any of the subscore changes between the two groups except for the GSRS pain and indigestion subscores, which decreased more in the cholecystectomy group than the hernia group (-0.59 vs. -0.10 and -0.43 vs. -0.13 respectively; $p<0.001$ and $p=0.03$). 63% of cholecystectomy patients exhibited a drop in GSRS pain subscores after the surgery, compared with 35% of hernia patients ($p<0.001$). The mean GSRS reflux subscore decreased by -0.32 in the cholecystectomy group and -0.05 in the hernia group ($p=0.12$). About 44% of cholecystectomy patients exhibited a drop in the reflux subscore versus 37% of controls ($p=0.005$).

Pre- and post-surgery GSRS constipation subscores were similar in the two groups, but pre- and post-surgery diarrhea subscores were higher in the cholecystectomy group (Table 3). GSRS diarrhea and constipation subscores did not change significantly after surgery. There

were no significant differences in the proportion of patients with decreases in constipation or diarrhea subscores between the two study groups.

Because of the different gender makeup in the two groups, we stratified the data by gender. At baseline, GSRS reflux subscores were generally higher in cholecystectomy patients than hernia patients for men but not women (for men, 2.04 vs. 1.39; $p=0.003$; for women, 1.83 vs. 1.59; $p=0.24$). For men, the GSRS reflux subscore decreased by -0.24 in the cholecystectomy group and -0.03 in the hernia group ($p=0.24$). For women, the reflux subscore decreased by -0.37 in the cholecystectomy group and -0.12 in the hernia group ($p=0.26$). At baseline, GSRS pain subscores were higher in cholecystectomy than hernia patients for both men and women, as expected (for men, 2.19 vs. 1.52; $p<0.001$; for women, 2.44 vs. 1.90; $p=0.01$). For men, the GSRS pain subscore decreased by -0.49 in the cholecystectomy group and -0.09 in the hernia group ($p=0.02$). Similarly, for women, the pain subscore decreased by -0.64 in the cholecystectomy group and -0.12 in the hernia group ($p=0.02$). Thus, the cholecystectomy and hernia groups exhibited similar decreases in pain subscores after surgery in men and women. Stratification of the data by hospital did not change the GSRS results (data not shown).

Patients with no baseline reflux symptoms, who started off with a GSRS reflux subscore of 1, exhibited a slight rise in GSRS reflux subscores after surgery ($+0.12$ for cholecystectomy and $+0.17$ for hernia surgery; $p<0.01$ for both). In contrast, patients with baseline reflux symptoms, who started off with a GSRS reflux subscore >1 , showed a significant drop in RSS after surgery (-0.63 for cholecystectomy and -0.37 for hernia surgery; $p<0.001$ for both). However, there were no significant differences when we compared pre and post-surgery changes between the cholecystectomy and control groups ($p=0.59$ for patients without baseline reflux; $p=0.27$ for patients with baseline reflux).

Regression Analysis

Multiple linear regression was performed using the quantitative change in RSS or GSRS reflux subscore as the dependent variable. Input variables included patient gender, age, surgery type (cholecystectomy or hernia repair), smoking, alcohol, and caffeine intake, and acid suppressive medication use. The analysis showed that none of the factors were independently associated with RSS or GSRS reflux subscore changes (data not shown).

Multivariate logistic regression was also performed using a decrease in RSS or GSRS reflux subscore as the binary dependent variable, together with the same input variables. Again, none of the input factors were shown to be independently associated with a decrease in RSS or GSRS reflux subscores (data not shown).

Discussion

Up to 50% of patients have residual or new symptoms after cholecystectomy, a phenomenon termed the “post-cholecystectomy syndrome”¹⁰, although there is controversy as to whether this syndrome actually exists as a distinct clinical entity¹¹. While incorrect preoperative diagnoses or inadequately treated biliary conditions may account for some of these post-cholecystectomy symptoms, the development of new pathology may also be a contributing factor.

A relationship between cholecystectomy and gastroesophageal reflux disease has been anecdotally described. The mechanism for this purported phenomenon is unclear. It has been postulated that after cholecystectomy the reservoir function of the gallbladder is lost, causing bile flow to be continuous rather than intermittent^{12, 13}, which leads to changes in the levels of gastrointestinal hormones^{14–16}. This in turn results in qualitative changes in the

composition of bile and more frequent transient lower esophageal sphincter relaxations¹⁷. Cholecystectomy can also induce duodenogastric reflux, which often manifests itself as a “gastric alkaline shift”^{18–26}. Duodenogastric reflux may result in symptoms similar to that of gastroesophageal reflux^{27, 28}. Furthermore, there is evidence to suggest that duodenogastric reflux can increase parietal cell density and gastrin levels, which can lead to transient declines in gastric pH²⁹. An alternative explanation is that after the resolution of biliary symptoms following cholecystectomy, some patients may resume consumption of a high-fat diet or gain weight, leading to worsened reflux symptoms. Other possible factors include the alteration of upper gastrointestinal motility²⁴, increased prevalence of *Helicobacter Pylori* infection³⁰, impaired gastric emptying caused by duodenal adhesions and the effect of medications used during or following cholecystectomy.

Six previous studies have suggested a relationship between cholecystectomy and reflux symptoms. In 1987, a retrospective study assessed 918 patients who had undergone upper endoscopy, finding that the 125 post-cholecystectomy patients were more likely to have erosive esophagitis and duodenogastric reflux than 793 controls who had not undergone cholecystectomy³. This was followed by a small, uncontrolled prospective study that evaluated 37 Irish patients undergoing cholecystectomy using pre and post-surgery symptom questionnaires, pH testing and esophageal manometry. After cholecystectomy, the number of patients with pH-proven gastroesophageal reflux increased from 13 to 27, the average DeMeester score increased from 15.2 to 34.2, and the number of patients with esophagitis increased from 8 to 19². Nine patients had worsened or new reflux symptoms. Mean lower esophageal sphincter function, as measured by the sphincter function index, was decreased after cholecystectomy. The same investigators also performed a small retrospective cohort study on 53 post-cholecystectomy patients and 14 controls consisting of normal volunteers and patients with non-cardiac chest pain¹. The post-cholecystectomy patients had a higher mean DeMeester score and higher incidence of esophagitis and reflux symptoms, although only 14 had heartburn. Subsequently, a small randomized controlled study reported a greater incidence of heartburn in patients who had undergone open cholecystectomy than those who had undergone laparoscopic cholecystectomy⁶. However, a prospective cohort study on 28 open cholecystectomy and 22 laparoscopic cholecystectomy patients found that both surgical approaches worsened reflux to similar extents, as measured by DeMeester scores⁵. These two prospective studies did not include a control group of non-cholecystectomy patients. Finally, a retrospective study compared 212 cholecystectomy patients with 62 controls (outpatients with minor complaints unrelated to the gastrointestinal tract) using a symptom questionnaire and visual analog scale. It was found that post-cholecystectomy patients had a higher prevalence of frequent heartburn than controls (19.3% vs. 3.2%)⁴.

Although these findings are intriguing, all these studies had limitations in study design. Three of the studies were retrospective and thus vulnerable to selection bias and confounding^{1, 3, 4}. Of the three that were prospective, one was uncontrolled² and the other two compared open versus laparoscopic cholecystectomy but did not have a non-cholecystectomy control group^{5, 6}. Many studies had methodological problems such as the use of unvalidated symptom questionnaires^{1, 2, 4–6}, excessive drop-out of subjects during follow-up⁵ or poor diagnostic criteria, such as making the presumptive diagnosis of “duodenogastric reflux” based on “large amounts of bile-colored secretions. . . noted in the stomach at endoscopy”³. Some studies had very small sample sizes^{1, 2, 5}. It should also be noted many of the studies were done on patients in Ireland, England and Finland^{1–3, 7}, therefore the results cannot be readily generalized to Americans because gallstone epidemiology may vary amongst countries.

The only prospective controlled study to date with a non-cholecystectomy control group was a small trial consisting of 17 patients and 11 controls. In this study, only three patients

reported new symptoms after cholecystectomy, and there were no differences in pre and post-cholecystectomy esophageal acid exposure on pH testing⁷. Compared to the non-surgical controls, the cholecystectomy group appeared to have higher DeMeester scores both before and after surgery (9.5 and 8.9 respectively versus the control value of 4.5), but these differences were not statistically significant, perhaps due to small sample size. Duodenogastric reflux, measured using gastric bilirubin testing and alkaline shift, was increased in six patients, but again there was no significant difference. Unfortunately, the conclusions we can draw from this study are limited by its small sample size, the absence of formal symptom assessment by validated questionnaire, and the fact that the controls did not undergo any surgery at all.

Our current study shows that cholecystectomy does not lead to an increase in reflux symptoms. In contrast to most previous studies, for both the cholecystectomy and hernia groups there was a modest improvement in reflux symptoms after surgery in patients who started off with some baseline reflux. As expected, GSRS pain and indigestion subscores decreased more after surgery in the cholecystectomy group than the controls, because abdominal pain and indigestion were indications for cholecystectomy in the first place. Our study has certain advantages over previous studies: 1) It is the only large prospective controlled study that used a non-cholecystectomy control group, with a sample size determined by an *a priori* power calculation; 2) It focused on reflux and other gastrointestinal symptoms and used two well-validated symptom questionnaires; and 3) It is the only study to feature a control group that underwent a non-cholecystectomy, non-gastrointestinal surgical operation.

However, our study also has several important limitations. First, because of the different epidemiological pattern of gallstone disease and inguinal hernias, there was a major difference in gender distribution and a small difference in age distribution between the cholecystectomy and hernia groups. Cholecystectomy patients were also less likely to be heavy caffeine takers and more likely to be regular users of proton pump inhibitors. However, when we stratified the data by gender, there were no changes in our results, while extensive multivariate regression analysis did not show any factors that independently predicted a decrease in reflux symptom scores.

Second, the time window for the return of our post-surgery questionnaire is rather wide (4–12 weeks). When we designed the study, we allowed for a wide time window because we anticipated that some subjects would require multiple reminders before returning the second questionnaire and we wanted to make sure that we captured as many subjects as possible. We felt that post-surgery symptoms would probably stabilize by 4 weeks, although it must be admitted that the available data on the time course of post-surgery symptoms are limited and it is possible that there might be a difference between the 4-week time point and 12-week time point.

Third, the absence of objective measurement of intraesophageal acidity with pH testing in our study raises the concern that some patients with reflux-like symptoms may not actually have true acid reflux because the correlation between reflux symptoms, actual pH change (objective testing) and esophageal mucosal damage (endoscopic findings) is known to be far from perfect^{31, 32}. For the purposes of our study, we were primarily interested in all reflux symptoms before and after surgery, whether caused by true intraesophageal acid reflux, alkaline reflux, bile reflux or other functional factors. From a practical standpoint, we felt it would be impossible to recruit large numbers of subjects if we required them to undergo pH tests or endoscopy both before and after surgery. Furthermore, our study was not funded to cover the costs of additional pH testing or endoscopy.

Fourth, obesity is known to be associated with cholelithiasis and acid reflux disease^{33, 34}, but not inguinal hernias³⁵. Therefore, it is possible that the cholecystectomy subjects were heavier than hernia subjects, but unfortunately weight data were not available for our study population.

Finally, even though we had performed an *a priori* sample size calculation, this was based on the premise that there would be an increase in reflux scores similar in magnitude to that reported by previous studies². As it turns out, not only was there no increase in reflux scores, but there was actually a trend towards decrease in reflux scores. Since none of the previous studies had reported a statistically significant decrease in reflux scores, it is unclear if our sample size was large enough to completely preclude the possibility of a type 2 error.

In conclusion, our data show that cholecystectomy does not lead to worsened reflux symptoms; in fact, there is a trend towards improvement. It has previously been suggested that if there is a true association between gastroesophageal reflux and cholecystectomy, patients already suffering from reflux prior to planned cholecystectomy should be considered for simultaneous cholecystectomy and fundoplication², a combined operation that is associated with a low complication rate and good post-operative course³⁶. Because gastroesophageal reflux and cholelithiasis are both common conditions and share certain risk factors, many patients may potentially be eligible for simultaneous cholecystectomy and fundoplication. However, our study raises important questions as to the appropriateness of this approach. Thus, simultaneous cholecystectomy and fundoplication cannot be recommended unless separate and independently adequate indications for both surgeries are present in the patient.

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Table 1

Demographic and lifestyle characteristics of study subjects.

	Cholecystectomy Patients	Hernia Patients	P-value
Mean Age	54.6±15.1	59.0±14.0	0.008
Male	36.8%	81.6%	<0.001
Smoking			
None	111	169	
<1 pack/day	6	14	0.49
1 pack/day	4	6	
>1 pack/day	0	2	
Alcohol			
None	42 (%)	49	
<1 drink/week	39	50	
<1 drink/day	30	66	0.12
2–3 drinks/day	12	26	
>3 drinks/day	1	5	
Caffeine			
None	33 (%)	41	
<1 cup/day	20	23	
1–2 cups/day	51	73	0.009
3–4 cups/day	20	44	
>4 cups/day	0	15	
Acid suppressive medications	27.2%	17.3%	0.035
Comorbid conditions			
Diabetes	10.4%	7.7	0.395
Coronary artery disease	6.4	12.8	0.068
Chronic obstructive pulmonary disease	8.0	7.7	0.910
Irritable bowel syndrome	9.6	8.7	0.692
Hepatitis B or C	1.6	2.0	0.776

Table 2

Changes in Reflux Symptom Score (RSS) values after surgery.

	Cholecystectomy Patients	Hernia Patients	P-value
Pre-surgery RSS, mean (SD)	1.44 ($\pm$ 1.86)	1.02 ($\pm$ 1.63)	0.04
Post-surgery RSS, mean (SD)	1.10 ($\pm$ 1.59)	0.88 ($\pm$ 1.38)	0.23
Change in RSS, mean (SD)	−0.34	−0.14	0.27
% with fall in RSS, mean (SD)	35% ($\pm$ 29%)	39% ($\pm$ 21%)	0.11

SD: Standard deviation.

Table 3

Changes in Gastrointestinal Symptom Rating Scale (GSRS) subscore values after surgery.

	Cholecystectomy Patients (±SD)	Hernia Patients (±SD)	P-value
Pre-surgery reflux subscore	1.91 (±1.29)	1.43 (±0.77)	<0.001
Post-surgery reflux subscore	1.59 (±1.02)	1.38 (±0.70)	0.05
Change in reflux subscore	-0.32 (-17%)	-0.05 (-3%)	0.12
% with fall in reflux subscore	44%	37%	0.01
Pre-surgery Pain subscore	2.34 (±1.16)	1.59 (±0.74)	<0.001
Post-surgery Pain subscore	1.76 (±0.84)	1.50 (±0.64)	0.02
Change in Pain subscore	-0.59 (-25%)	-0.10 (-6%)	<0.001
% with fall in Pain subscore	63%	35%	<0.001
Pre-surgery Indigestion subscore	2.32 (±1.29)	1.89 (±0.94)	0.01
Post-surgery Indigestion subscore	1.89 (±0.96)	1.76 (±0.83)	0.23
Change in Indigestion subscore	-0.43 (-18%)	-0.13 (-8%)	0.03
% with fall in Indigestion subscore	58%	43%	0.08
Pre-surgery Constipation subscore	1.91 (±1.11)	1.71 (±1.00)	0.11
Post-surgery Constipation subscore	1.67 (±0.79)	1.66 (±0.95)	0.94
Change in Constipation subscore	-0.25 (-12%)	-0.05 (-2%)	0.09
% with fall in Constipation subscore	39%	31%	0.67
Pre-surgery Diarrhea subscore	1.93 (±1.27)	1.42 (±0.72)	<0.001
Post-surgery Diarrhea subscore	2.05 (±1.21)	1.41 (±0.71)	<0.001
Change in Diarrhea subscore	+0.13 (+7%)	+0.01 (+1%)	0.28
% with fall in Diarrhea subscore	33%	25%	0.89

SD: Standard deviation. Bonferroni corrections have been applied to p-values.